**Clinical Immunology**

Host defenses:

1. Antibody Mediated Defense: Neutralization, opsonization, complement activation
2. Tcell Defense: CD8 (virus infected cells) CD4 (macrophage activation, Bcell activation)
3. NK Defense: killing of intracellular pathogen (balance activating receptor and KIR); cancer
4. Phagocyte Defense: Bacterial clearance (extracellular pathogen); ROS, lysozyme, peptidase, acid
5. Complement system: extracellular pathogens for phago or MAC

Bacterial Evasion strategy: mimicry, latency, down regulate receptors, offensive strategies, toxins

Diagnosis of infection vs colonization: culture catheter tip and the blood… >15 cfu and cocontaminant in the blood. Staph and candida… pull the catheter. Should pull the catheter always unless it is a patient with many catheters and then may consider keeping the catheter full of alcohol or antibiotic. Clean with chlorhexidine, sutureless, transparent dressing with chlohexidine, tephlon catheter, impregnated catheters.

IVIG: prepared from large pools of plasma until all IgG groups are present (1-4). It is an excellent method for treating Immunocomp patients

Bone marrow transplant: need to be ABO type matched and also check for allopathic antibodies of recipient against the host. Great method for treating any genetic ailment for complete T/Bcell loss.

Splenectomy: given for trauma, idiopathic thrombocytopenia purpura, spherocytosis, thalassemia, Lymphoma, and abscesses. Some diseases have functional hyposplenism: Graves, Hashimoto, Lupus, Sjogren, Lymphoma, CML, amyloidosis, Alcohol, Elderly/neonate, crohn, Sickle cell. See Howell Jolly bodies and pocks on the RBC. PT more susceptible to *S.pneumo, H. influenza, N. meningitides.* Give Pneumococcal poly, conjugate pneumococcal, H flu, Meningococcal(YWCA) Vaccinations.

**Immuno Defficiency**

Defficiencies are Primary (inherited) or secondary (acquired by infection, medical intervention, aging)

*SCID* (ADA defficiency, gamma chain mutation, RAG problem, CD3 mutation) is a clinical phenotype with a compromised immunity due to impaired Tcell devel and nonfunctional/absent Bcells. The patients present with opportunistic infections and pyogenic infections. Additionally, since they do not produce Tcells, they will not have a thymic shadow. All patients require a bone marrow transplant.

Tcell deficiencies have mycobacterial, nocardial, legionella infections. Cryptococcus, histoplasmosis, pneumocystis, Herpes, cryptosporidium and toxoplasma infections.

1. Xlinked SCID (T -, B r, NK -): **X-linked** mutation in the common gamma chain. IL2,7,15 all needed for Tcell survival and maturation. B cells cannt function without Tcell help and NK devel also depends on IL 2, 15. Opportunistic infections quickly overwhelm the unprotected infant. **Bone marrow transplant.**
2. ADA Deficiency and PNP deficiency (T -, B -, NK -): **AR** toxic metabolite accumulation due to a deficiency in ADA or PNP enzymes which are needed Adenosine or Guanine metabolism. This results in an increase in dATP which also causes inhibition of ribonucleotide reductase enzyme (neg feedback?) which is responsible for all deoxynucleotide production. ADA is ubiquitous in all tissues (lack of ADA causes rib flaring…) but ADA is mostlyin the Thymus. Thymocytes are more susceptible to destruction by adenosine metabolites. As a result, tcells will be destroyed and the infants are seen to lack a thymus. **Bone marrow transplant.**
3. SCID/Omenn Syndrome (T-,B-, NK+): **AR** defective Rag (1 or 2) which results in impaired V(D)J rearrangement. IF the Rag is non-functional = SCID. IF Rag is abnormal you can see more GVHD phenotype “omen syndrome” with rash, diarrhea, LN swelling. **Bone marrow transplant.**

Other Tcell/Bcell issues

1. Blooms Syndrome (T r,B r, NK +): defective DNA helicase (no DNA repair) and show increased susceptibility to respiratory infections. It is a mild SCID phenotype but presents at a later age, premature aging, photosensitivity, cancer predisposition. **Irradiate/chemo then bone marrow**
2. AtaxiaTelangectasia (T r, B r, NK +): **AR (often compound heterozygotes)** ATM gene mutation that results in a mild SCID phenotype. The ATM is also responsible for DNA repair and class switching. Sinopulmonary infections, premature aging, photosensitivity. Ataxia is the earliest sign (2-3yrs old) as well as dilated BV in eye/ear. **Irradiate/chemo then bone marrow transplant.**
3. Wiskott-Aldrich (T,B,NK but are all nonfunctional): **Xlinked** WASP gene mutation impacting actin polymerization; protein only expressed in Leukocytes and megakaryocytes. Without the protein, impaired of Tcell activation through the TCR and Thelper activation of Bcells. NK cell cytotoxic function is also impaired. Patients will show impairment of platelet function (small and ineffective) with susceptibility to opportunistic and pyogenic infections. **Prep then bone marrow**
4. DiGeorge(T r, B+,NK+): TBX gene (CATCH 22 Cadiac, Abnormal face, Tcells impaired, cleft palate, hypocalcemia) with impairment in the pharyngeal pouch development resulting in: Congenital heart problems, hypoParathyroid, hypocalcemia, and variable immunodeficiency. Complete versus incomplete depending on the mutation and its impact on Tcell development. Will have hooded eyes, bulbous nose, high palate, rotated ears. Will have general susceptibility. **Thymic transplant if complete syndrome.**
5. MHCI deficiency: **AR** TAP gene mutation (1or2) resulting in impaired CD8 activation. Sustained respiratory infections with chronic inflammation. *Bare lymphocyte syndrome*
6. MHCII deficiency: CIITa gene mutation that is responsible for transcription activation of MHC genes. Since MHCII is required for positive selection of CD4, there are low CD4 levels. This results in lack of Bcell activation and CD4 TH1 cell. Patients have opportunistic and pyogenic MHC II are all on APC so these will have impaired function. *Bare lymphocyte syndrome*
7. Xlinked Agammaglobulinemia: **Xlinked** Btk gene is necessary for B cell development from PreB to mature B. Development of Bcells halts at PreB stage in Btk mutations resulting in an absence of mature B cells. Patients show increased susceptibility to pyogenic infections and all antibody mediated immune infections (enteroviruses). NO LIVE VAX. **IVIgG**
8. Transient Hypogammaglobulinemia: low IgG levels at birth with a full recovery in months to years (all recover by age 3). PT show increased susceptibility to URT, OM, Bronchitis, meningitis infections.
9. Common variable immunodeficiency CVID: low levels of all Ig especially IgG. Normal numbers of Bcells… just that they produce low levels of soluble Ab. Increased Cd8. 15-25yo. Prone to malabsorption, autoimmune, large joint arthritis, GI, lymphoma. SX include sinopulmonary, chronic enteric, and severe viral meningitis/encephalitis/myositis. **IVIG**
10. Hypogammablobulineamia/ IgA deff: **AR** low levels of IgA but few complications. Often associated with CVID and rarely can cause upper/lower resp infections or dietary infections.
11. Xlinked Hyper IgM: **Xlinked** Mutation in the CD40L gene resulting in the impairment of Bcell. activation by Tcells. No Isotype switching so compensation by increased IgM from TI activation of B cells. CD40 L on the Tcell and CD40 on the B cell and macrophages. These patients show increased susceptibility to pyogenic and pneumocystis and cryptosporidium. **IVIg**
12. Activation induced Cytidine Deaminase (AID): **AR** AID gene (UNG gene too) mutation resulting in the impairment of the somatic hypermutation and class switch. VDJ switch depends on RAG. These patients will only show susceptibility to pyogenic infections. The patients will only produce IgM (these have low affinity since they do not undergo somatic hypermutation) and will produce larger numbers of IgM.
13. Xlinked Hypohydrotic Ecotdermal Dysplasia with ID: NEMO gene mutation (NF-kB essential modulator) or known as IkB. This gene involves Macrphages activation by TNFalpha and also Tcell activation of Bcells. With this impairment, there is a decrease in immune response by macrophages as well as no isotype switching. PT have recurrent infections and abnormal sweat gland, hair and teeth development.
14. Xlinked lymphoproliferative Syndrome: SH2 domain containing gene 1A to encode SLAM associated protein (SAP). SH2S1A makes SAP which interacts with cytoplasmic tail of SLAM in Tcells and NKcells leading to production of INF gamma. The SH2S1A gene is mutated resulting in defective activity of Tcell and NK, faulty cytokine production and uncontrolled prolif of lymphocytes. This causes Bcell lymphoma. *EBV driven tumors*
15. NK cell defect: usually needed to kill cells that down regulate MHC I (herpes viuses). Patients that lack the NK will have impaired ability to resist herpes viruses.

Neutropenia (Drug induced or hereditary): Many neutrophils are produced daily and have an 7 hour half-life. Mild/moderate/severe forms include 1000-1500, 500-100 and below 500. Patients are very susceptible to GNB with high mortality in febrile infections. Recovery requires the return of normal number and function to neutrophils. Note that ME and Africans show lower normal rates for neutrophils. MOST infections disseminate from the bloodstream (sepsis was mostly from the lung).

1. Leukocyte Adhesion Deficiency: Mutation in the CD18 gene that normally combines with CD11A,B,C to make LFA-1, CR3 and CR4. LFA1 is involved in leukocyte migration and CR3 and 4 are involved in phagocytosis of iC3b. Result: recurrent pyogenic infection, longer healing times to trauma, increased fungal infections. **Bone marrow**
2. Chronic Granulomatous Disease: **Xlinked** Problems with the NADPH oxidase (necessary for SOD production) so that microbes can be phagocytized but not degraded. Causes chronic infection and granuloma formation. Seen in the first year of life. **Treat with IFN gamma but need transplant. *DHR test is better than NBT and these PT wont have strep infections.***
3. Myeloperoxidase def: MPO used to convert H2O2 to HOCl. As a result, decreased bleach production leading to an increase in susceptibility to fungal infections (candida). Often associated with diabetes.
4. Chdiak Higashi: **AR** LYST gene mutation needed for lysosomal trafficking. PT have large dysfunctional neutrophils. Melanocytes, schwann cells, renal, thyroid are all effected. PT have patchy melanin deposition, low IQ, susceptible to bacterial infections and even after a bone marrow transplant, have severe neurodisorders.
5. Hyper IgE (job’s syndrome):Stat3 gene mutation. Mostly white females and VERY rare. Problem with IFNgamma response in neutrophils where constant staph skin abscesses, sinusitis, OM, pneumo, eczema, typical faces, scoliosis and can have 2 rows of teeth.
6. Hereditary Cyclic neutropenia: **AD** rare and due to ELA2 mutation. PT experience episodic neutropenia every 2-5 weeks. Cycles are HIGHLY predictable and SX include malaise, skin ulcers, fevers for 5-8 days that spontaneously resolve.
7. Acquired Neutropenia: post infection in children, chronic infections (MTB, Leishmaniasis, brucellosis), sepsis, Antibiotics/antifungals, chemo, diuretics, Anticonvulsants, Antiinflam, Antithryroid.
8. Mucositis: may involve the entire GI tract with consistant recurrent Strep/Enteric bacteremia. Patients with radiation, transplant, chemo all are susceptible. Keratinocyte growth factor seems to help though mouth antiseptic/anesthetic rinses are the best.
9. Ecthyma gangrenosum: Mostly Pseudomonas with invasion of vessels and NF. Can be seen with extensive infarction in other organs (lungs). Characteristic lesions without puss.
10. Typhlitis AKA necrotizing entercolitis: fever and inflammation of the cecum with a mix of gram negative, anaerobes and candida. High mortality due to bowel perf but DO NOT OPERATE until the bowel actually perforates.
11. Disseminated Candidiasis: can be seen with neutropenia that also includes TPN and a history of broad spectrum antibiotics. PT has many ulcers everywhere that are not really ulcers or abscesses because no pus. Affects many organs with poor TX response

**Secondary Immune diseases**

1. Diabetes mellitus: decreased neutrophil function from increased glucose; increased fungal infections and NF by pseudomonas in external otitis; cardiovascular compromised
2. Dialysis: reduced T cell function, decreased Ab, compromised Neutrophil/dendritic cells; high levels of IL2; peritoneal dialysis often susceptible to bacterial perotinitis
3. Nephrotic syndrome: loss of Ig and complement; treat with glucocorticoids; perotinitis by pneumococcus and E.coli are frequent.
4. Cirrhosis: reduced clearance of glucocorticoids; shunting portal blood and decreased protein production (complement proteins); kupffer cells become less active due to reduced complement leaving the PT subject to bacterial infections
5. PT on TNF monoclonal antibodies: anti TNFalpha in RA have a high risk of TB and histoplasmosis as TNF needed for macrophage activity and signaling.

**Nosocomial infections:**

Infections are clinically evident in 48hrs. ICU and nurseries have the highest risk. UTI, surgical sites and pneumo are the most common. There are three factors: iatrogenic, organizational, patient related. Isolate for contact, resp, droplet or reverse. MRSA, VRE, Cdiff, MDRO are isolated for contact; Tub, varicella, measles are isolated for resp; meningitis, mumps, influenza are isolated for droplet. Clean hands, clean site, gowns/goggles/gloves, antimicrobial stewardship, avoid bad drugs, minimize invasive procedures and improve patient spacing or cohort infectious patients.

1. MRSA: staph infection that is oxacillin resistant
2. CAMRSA: carries a PVL toxin… often infects resp after a viral infection
3. Vanco resistant Entero faecium: hardy and mostly Europe. Mostly ICH with urinary cath colztn
4. C diff: clinically significant diahrea for 3 days with history of antibiotic use.
5. UTI: most often related to catheter. Ecoli, kelb, pseudomonas, entero, candida, staph saprophy
6. Blood stream: central venous cath (femoral>jug>subclavian) with mostly GPC, then GNB (pseudomonas 33%), and some fungal like candida
7. HealthCare Associated Pneumonia HCAP: often associated with ventilators and increased risk in ICU. Nasal intubation, naso-gastrictube, supine, large gastric volume, malnutrition…. Mostly MRSA, pseudomonas, acinetobacter, enterobacter, kleb, legionella.
8. Ventilator associated Pneumo:Head up, subglottic suction, avoid gastric distension, decontaminate mouth, remove tube asap,
9. Surgery site infection: often gram positive from PT natural floura. SCIP is now being implemented where have to report cases, data is public, prescribe the right Abx 1hr pre and remove 24hr post; clip hair and avoid intraoperative hypothermia. Vertical targeting: MRSA screening/decolonizing; horizontal screening: chlorohexidine wash; always use sterile technique.

Respiratory infections

1. Common Cold (Rhinitis): self-limited, runny nose, cliated cells affected but little damage. Sx peak in 3-4 days and can last 1-2wks. Mostly Rhinovirus then Paraflu, RSV, corona
2. Pharyngitis: most common illness seen by PCP. 30% viral are mostly rhino, adeno, corona, HIV; 30-40% bacterial are mostly Strep; the rest are unknown. SX fever, chills, exudate, lymphadenopathy
3. Laryngitis: viral infection with hoarseness, dry cough by mycoplasma, chlamydia, strep
4. Acute Bronchitis: persistent cough, flu-like, can progress to adult onset asthma (walking pneum)
5. Influenza: leading infectious cause of death in the USA. Epidemics come 1-3 years, Pandemics come on the decades. H and N variations can cause genetic shifts. Significant runny nose, fever, cough, malaise. Influenza can lead to pneumo as a primary complication or secondary.
6. Viral Pneumonia: by influenza or RSV
7. Bacterial Pneumonia: mostly GNC (strep pneumo), aspiration with rigor/chills/chespain, rust colored sputum in late stages and usually only one lobe. Need cephalosporin often since more and more resistance to pen. Bacteremia and death can occur in splenectomized patients. Kelb pneumo, Staph can also cause pneumo
8. Atypical Pneumoia: mycoplasma causing walking pneumonia with bronchitis, HA, dry cough, sore throat but positive CXR and cold agglutins. Need azithro or tetracylines. Note that Chlamydia can also cause similar symptoms
9. Aspiration pneumonia: pneumonia from normal mouth flora being inhaled… inspect dentition, lobes dependent on patient position, gramstain shows GP and GN of various forms; often seen with alcohol, sedation, anesthesia, stroke, seizure…

**Abdominal infections**

1. Vibrio Cholera (16-72hrs): ctxAB ribosylates Gs to increase CAMP production (decreased Na absorption, increased Cl secretion). Secretory diarrhea that does not necessarily need Abx as it is not invasive and rarely causes a fever. The toxin is encoded on a phage and many other organisms have cholera-like toxin. Often from shellfish, acid sensitive, endemic to Gulf, Latin A., Africa. Only in humans and has “rice water”diarrhea in the worm months. NO person to person but by consumption.
2. Vibrio parahemolyticus: explosive diarrhea in 24 hrs with N/V and abdominal cramps. Headache, low fever and self limiting. It is the #1 cause of seafood gastroenteritis. Hemolysin is responsible for the chloride secretion and tissue damage. Requires salt for growth (septicemian and wound infections in the warm months).
3. Vibrio vulnificus: protein capsule to protect, sepsis after eating oyers. **SX** diarrhea, N/V and cramps. Problematic in immunocomp patients with bacteremia, fever, chills, skin leasions (even necrotizing fasciitis). #1 cause of seafood related deaths.
4. Enterobacteriaceae (usually within 24hrs): g(-) rods, most are motile (not shigella, kleb, yersinia) and most ferment lactose (CSEEK). Ecoli, kleb, proteus are all opportunistic.
   1. ETEC­: mostly seen in travelers and weanlings. Acid sensitive, secretory, food contamination with LT or ST toxins. The LT is like cholera and the ST is like Yersinia (cGMP). Maybe give antibiotics??? But bismuth can prevent.
   2. EPEC: Infant diarrhea with effacing of the microvilli. ). No inflammation or fever as the diarrhea is mediated by a decrease in aquaporins, and altering actin pol in microvilli resulting in an effacing lesion with pedestal.
   3. EHEC: O157:H7 with shiga toxin for bloody diarrhea from damage to the ascending/transverse colon. It is the number one cause of HUS (prob by DIC) in kids under the age of 10. Often in Lamb or beef. Culture the stool on SMAC.
5. Invasive Enteric pathogens: also known as dysentery with low volume/high frequency stools containing puss and blood.
   1. Shigella (16-48hrs): dysenteriae (most common), sonnei (USA)… only really infect humans. HIGHLY acid resistant and spread by contact, food, sex. Endemic to male homosexuals. Very acid stable and similar to *EIEC Enteroinvasive Escherichea coli.* Person to person contact and sometimes from a contaminated source. Bacteremia is uncommon though the shiga toxin is the cause of symptoms. Microbe enters the M (microfold) cells of the colon by invasin binding to an integrin. They then pass into the lamina propria where some are ingested by macrophages which release IL-1 (crucial for the host to cause pathogenic diarrhea). The inflammation loosens the tight junctions increasing the permeation by the microbe and attachment to the basolateral aspect of the epithelial mucosal cells for endocytosis (hemolysin allows to escape phagosome). ABM to spread to neighboring cells (like listeria, burkholderia). Shiga toxin halts 60S ribosome so no protein synth.
   2. Salmonella (16-48hrs): Part of the normal flora of many animals and is spread by fecal oral spread. Acid sensitive and travel to the ileum and colon where they attatch and penetrate the mucosal barrier. They do not remain in the epithelial cells but pass into the blood to multiply in the macrophages of the liver and lymph nodes. Once a threshold is reached, they are released back into the blood (secondary bacteremia) where they cause the continuous bacteremia and daily fevers for 4-8 weeks. Infected individuals (give ampicillin, ceftriaxone and Bactrim):
      1. Carriers
      2. Gastroenteritis: *S.enterica* causing N/V/D (from chicken)
      3. Vascular endothelial infection: *S. choleraesuis, typhimurium*
      4. Typhoid fever: *S.typhi* and *paratyphi AandB (*human carrier)Particular ogan infection: *S.typhimurium* causing osteomyelitis in sickle cell
   3. Yersinia: entercolitica (16-48hrs) and pseudoTB are primary enteric pathogens that resist phagocytosis. Typical infection is by consumption of contaminated food (can grow at 4C). Seen in Belgium, transfusion, may mimic appendicitis. Common to NEurope and Canada. PT have fever and mesenteric adenitis with a duration of 24hrs to 14days.
   4. Helicobacter: spiral gram negative rod with corkscrew motility, urease and adhesins. Associated with chronic gastritis, gastric cancer and MALT. Fecal oral transmission and can be tested for my the urease test.

Food-borne Disease

1. Staph aureus (2-6hrs): *Food poisoning:* [2-6 hrs] with enterotoxin A or B in foods left at room temp. Abrupt salivation, N/V/D, community outbreak and self limiting. Ham, poultry, egg salad and pastries.
2. Baccilus cereus (2-6 hrs/ 8-16hrs): spores found everywhere. Common cause of food-borne intoxication with transient, self-limiting illness of 12-24hrs. **SX** Short incubation is 1-6 hours with nausea, vomiting, cramps and due to the toxin… not the bug (Looks like *Staph. Aureus*). Associated with milk, rice, pasta. Long incubation caused by consumption of spores followed by heat-labile enterotoxin production in the small intestine. These include camps and diarrhea within 8-16 hours due to increased cyclic AMP. Occular infection following trauma of the eye and blindness in 48 hours (*B.thuringiensis* can also cause this).
3. Clostridium perfringens (8-16hrs): only from the type A strain and causes diarrhea. Comes from raw meat and the HT enterotoxin damages the brush border epithelium with net secretion of Na and fluid.
4. Camplobacter jejuni (16-48hrs): most common chicken/raw milk contamination. Causes dysentery. Is associated with ascending paralysis of GB.
5. Lysteria (16-48hrs): can occasionally be in the normal host and causes watery diarrhea.
6. Norovirus (1-2days): THE MOST COMMON FOOD BORNE pathogen with V/D and fever (33%).
7. Clostridium botulinum (lontest): acute GI symptoms within 18-36 hours (due to the toxin) causing neck down paralysis… AB toxin that targets the Ach receptors.
8. Nonbacterial toxin/virus (5-15min): NV with cramps…
   1. heavy metals (copper, zinc, tin, cadmium);
   2. cryptosporidium is a fungus that can often cause gastrointestinal issues (diarrhea)
   3. Chinese restaurant: parasthesia in 1hr from MSG poisoning
   4. Niacin poisoning with para in 1hr
   5. Histamine from fish: tuna/mahimahi with buring mouth, flushing, dizzy, NV with p1hr
   6. Baracuda/snapper: numb tongue/lips and sharp shooting pains in the legs, sensation of your teeth being loose. Hawaii-florida… parasthesia in 1-6hrs.
9. Mushrooms: Botenic acid (mimics EtOH), Muscarine (parasymp hyperRx), Psilocybin (psychosis), amatoxins (gastro, liver/kidney failure)

**Urinary Tract Infections** (most common nosocomial, bacterial infec in elderly, causes bacteremia, rarely fatal). Protection: urine itself (low pH/glucose, high urea), neutrophils in mucosa, epithelial cells recognize and recruit, tamm-horstfall protein, bladder mucopolysaccharide, urine flow, valves/length, distal urethral colonization. Lower = cystitis, urethritis, prostatitis. Upper= pyelonephritis, renal abscess. Uncomplicated UTI: woman, middle aged, healthy, not pregnant, not sick, normal anatomy.

* Sterile pyuria: consider TB
* Girls under the age of 5 and boys… if UTI, suspect an anatomical issue
* Fungi are usually contaminants but candida can cause bacteruria in DM
* Serratia has a red pigment
* Proteus uses urea as an energy source and can be found in struvite stones
* Staghorn calculi can harbor bacteria in the bladder to serve as a source of chronic infection.

**Congenital infections:** mothers are often asymptomatic; severity is linked to early infection; congenital infection is often more severe than the same infection in the adults. Transplacental transmission can result in fetal loss, premature, slow growth, persistant neonate infection. **TORCH (toxoplasma, other syphilis, HIV, Hep C/B, rubella, cmv, herpes simplex)**. These are the most common in oder:

1. CMV (T): primary infection of the mother has 40% chance of transmission of which 15% show significant neurologic sequelae. Secondary infections only have a 1% chance of transmission to the baby since the mother already has a significant number of Ab to the virus. At risk moms are those that do not wash their hands and are regularly in contact with children. **Dx: periventricular calcifications.**
2. B19 (T): fetal hydrops…
3. Hep B/C (I): hepatitis
4. HSV (I): specific to the 3rd trimester; transmission can be avoided by C-section delivery. It is a very serious infection in the new borne that needs immediate treatment. Meningitis, disseminated form, vesicle/mucocutaneous.
5. HIV (I/T): baby can also be infected by consumption of breast milk. Need immediate therapy and the baby usually responds very well.
6. Rubella (T): largely eliminated in the US. >50% risk of contracting if the mother is infected. Most severe symptoms include PDA and MR as well as cataracts.
7. Toxoplasmosis (T): not acutally 7th most common but does cause transplacental infection. If infected… wait 7-9months to get pregnant. This is from cat feces or contaminated pork. 50% infections are asymptomatic. Newborns need aggressive treatment. Will have eyesight issues that manifest in their teenage years. **Dx: diffuse cerebral calcification.**
8. Syhilis (T): need to test and treat moms (even if allergic to pen…) since many different complications including bone lesions even in 20% of nonsymptomatic babies. Need to do a CSF screening if baby borne to a seropositive mom. No infection during the first 10 weeks of pregnancy (provides a treatment window); early pregnancy infection results in miscarriage; late pregnancy infection causes moon’s molars, congenital defects, skin lesions, bone deformation…
9. Group B strep: perinatal infection; 50% will be colonized and 1-2% develop the infection. Majory concern is the possibility of developing sepsis or meningitis in the newborn.

**Skin/Bone infections**

1. Cellulitis: infection of the dermis and SubQ tissues (staph a/strep p) as a result of a break down in the stratum corneum barrier. This barrier is usually dry, salty, low pH, tough and filled with langerhan cells. Edema secondary to heart failure/lymphedema due to blockage can cause reduced flow to the skin and are risk factors for the disease. DM and lower extremities without veins (post CABG) are also at risk. Lastly, immune deficiencies are also risk factors. Staph produces alpha toxin and leukocidins to kill neutrophils. Strep has M proteins to escape/evade immune cells.
2. Onychomycosis: fungal infection of the fingernails that can serve as a risk factor for developing cellulits. The fissures caused in the skin by fungus (candida or dermophyte) or by chronically wet skin that would harbor fungi.
3. Stasis dermatitis (lipodermatosclerosis): chronic venous insufficiency results in: decreased sensation, red/yellow skin color change, areas of chronic inflammation and those with fibrosis, cool cellulitis… this is a risk factor for skin infection and not an infection in itself. Trapping of fibrin outside the vessels cause fibrin cuffs; chronic inflammation with tissue hypoxia; venous hypertension with decreased lymph flow. All result in damage to the microlymphatics with increased fluid stasis.
4. Paronychia: nail infection at the cuticle or at the site of a hangnail
5. Felon: infectious abscess of the finger-tip and finger pad… as it expands it can impinge the local circulation or spread to the bone.
6. Impetigo: (strep) localized and purulent infection of the epidermis in children with poor hygiene. Mostly in summer months of a northern climate or all year in a tropical climate. Colonization of the skin (10days and asymptomatic) followed by invasion after trauma. The papules become pustule with a honey colored exudate (staph bullous impetigo has a clear crust).
7. Erysipelas: group A strep… deep infection of dermis following pharyngitis. **SX** acute inflammation with lymphatic involvement (face, trunk, extremities but the face is the least problematic). Visible, raised, advancing red margins. Can be fatal and treated with penicillin.
8. Folliculitis: infection of the hair follicle
9. Furuncle/carbuncle: starts at the base of a hair follicle and then more than one lesion connects by way of tunnels under the skin.
10. Periorbital (Preseptal) and orbital (postseptal) cellulitis: Pre is more common, milder, stap/strep, vision is fine. Post is more rare, with sinusitis, higher morbidity, pneumococcu/mixed/fungi, 10% lose their vision… may need surgery.
11. Septic cavernous sinus: abrupt onset diplopia, photophobia, orbital swelling, exophthalmos… secondary to infection. Rare but needs surgery because of high morbidity. DO NOT anticoagulate and steroids do not help.
12. Necrotizing fascitits: Involves the superficial fascia and secondary to a minor trauma/surgery or even furuncle. Type 1: mixed flora with anaerobes + strep (nongroupA) and gram neg. Type 2: Group A strep. Type 3: Clostridium perfringens with gas gangrene or clostridial myonecrosis. Feel the crepitus to diagnose, control the spread, PT will be septic shock and very ill, need immediate debridement. Mortality is 30%.
13. Zoster: caused by reactivation of chicken pox. Usually a dermatomal pattern but in rare instances of severe ICH, the PT can have multidermatomal, extensive, disfiguring and recurrent infection. Post therapeutic neural neuralgia can be debilitating. Be wary of Staph super infection. Give te VSV to old, immunocompromised, transplants.
14. Bites: Staph, Eikenella (human), Bacteroides, Prevotella, Porphyromonas, Pastuerella… need Abx and treatment for rabies and tetanus.
    1. Pasteurella multocida: rapid swelling, arthritis, septicemia, endocarditis. TX amp/sulbactam.
15. Toxins: TSS typically by Staph aureus, but strep and n.meningitidis can cause something similar. TSST-1 toxin is a super antigen binding non-specifically to Tcells to active 20%!!!! Multiorgan failure due to sever vasodilation and edema. Additionally the agr gene (toxin) is activated when increased protein, neutral pH and changes in O2 and C02. 95% of people have antibodies by 40yo. Also causes scaled skin syndrome by staph A and b. Scarlet fever (strep pharyngitis) with sandpaper rash with strep pyrogenic toxins with circumoral palor.
16. Bone infections: usually bacterial and rarely is it fungal. It is the leading cause of amputations in the US. Adults have contiguous spread while children are usually hematogenous spread. Diabetes, vasculopathy, invasive procedures, trauma, drug use are all factors. Diagnose if there are ulcers, positive probe-bone test, ESR, abnormal xray. WBC and platelets can be completely normal in these cases. Nuclear medicine can help but still needs more work. Sequestrum is the tissue within the bone abscess (involucrum). Can also do a bone biopsy. Think Staph aureus, strep B, Ecoli, Group A strep, Haemophilus is now rare, Pseudomonas for IVDU, Salmonella for sickle.

TIPS: fresh/brackish water is filled with Aeromonas, Plesiomonas; salt water has vibrio vulnificus; fish tanks hold mycobacterium marinum; meat/fish esposure to damaged skin will have erysipelothrix

